

Clean Copy of the Amended Specification:

Page 73, replace with the following:

population of 1,010 individuals was also evaluated. Analysis by SSCP and DNA sequencing revealed 3 abnormalities and 1 polymorphism.

Q9E-hMiRP1. One of 20 patients with drug-induced arrhythmia had a C to G transversion at nucleotide +25 (nucleotide 98 of SEQ ID NO:1) of *hKCNE2* producing a Q9 to E substitution in the putative extracellular domain of hMiRP1. This mutation was not identified in 1,010 control individuals. The patient is a 76 year old African American female with a history of high blood pressure, non-insulin dependent diabetes and stroke. Two baseline electrocardiograms showed QT intervals corrected for heart rate that were borderline prolonged (QTc = 460 ms). Echocardiography revealed concentric left ventricular hypertrophy with mild to moderate diffuse hypokinesis but no ventricular dilatation. The patient was admitted to the hospital with pneumonia and treated with 7 doses of intravenous erythromycin, 500 mg every 6 hours and then switched to oral clarithromycin, 500 mg every 12 hours. After 2 doses of clarithromycin electrocardiography showed a QTc of 540 ms. The patient developed TdP and VF, requiring defibrillation. At the time, she was hypokalemic with a serum potassium level of 2.8 meq/L.

M54T-hMiRP1. One of 230 patients with inherited or sporadic arrhythmias had a T to C transition at nucleotide +161 (nucleotide 234 of SEQ ID NO:1) causing substitution of M54 to T in the predicted transmembrane segment. This mutation was not identified in 1,010 control individuals. This patient is a 38 year old Caucasian female who was in good health. She was on no medications. This individual had VF while jogging. Her resuscitation required defibrillation. The results from echocardiography and cardiac catheterization with electrophysiologic studies and right ventricular biopsy were normal. Subsequent electrocardiograms showed an atypical response to exercise with QTc intervals ranging from 390 to 500 ms. An automatic internal defibrillator was placed.

I57T-hMiRP1. Another of the 230 patients with inherited or sporadic arrhythmias had a T to C transition at +170 (nucleotide 243 of SEQ ID NO:1) causing an I57 to T substitution in the predicted transmembrane segment. This patient is a 48 year old Hispanic female who is in good health and has no history of TdP or VF. Her resting electrocardiogram shows a prolonged QT

interval (QTc = 470 ms). She is a member of a multi-generational family now under genetic, clinical and biophysical evaluation.

A' *T8A-hMiRP1*. In 18 out of 1,260 individuals screened, an A to G polymorphism at nucleotide +22 (nucleotide 95 of SEQ ID NO:1) produced a T8 to A change in the putative extracellular domain of MiRP1. The
